

THE ROLE OF PRODUCTS OF FOOD DIGESTION IN THE STIMULATION OF PANCREATIC SECRETION

I. V. Malkiman

Laboratory of the Physiology and Pathology of Digestion (Director – Prof. S. I. Filippovich)
Institute of Normal and Pathologic Physiology (Director – Active Member AMN SSSR V. N. Chernigovskii) AMN SSSR, Moscow

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In his first independent experimental work on digestion, which was devoted to investigation of the mechanism of the second phase of gastric secretion, I. P. Razenkov posed the question concerning the role of the products of peptic digestion in the stimulation of the secretory activity of gastric glands. Further investigations in this direction carried out by I. P. Razenkov and his collaborators led him to conclude that the chemical stimuli in the form of foodstuffs and products of their digestion, especially products of protein digestion, were able not only to stimulate gastric secretion but were also a powerful factor affecting the activity of various organs and tissues, among them the digestive organs. I. P. Razenkov ascribed great significance to the role of humoral factors in the process of adaptation of the body to its environment and correlation of function between organs, and has repeatedly stressed that they act most frequently through the nervous system. This was particularly clearly formulated by him on interpretation of the change in the ratio of the magnitude of the first and second phase of gastric secretion when the animals were kept on a prolonged bread or meat diet.

The work of I. P. Razenkov which is most closely related to the present study is that on the mechanism of secretin formation. The experiments carried out by I. P. Razenkov et al. [2, 3] showed that peptone, gastric juice and products of digestion of fibrin, meat and milk played a substantial part in the mechanism of secretin formation in the duodenum. However, whether the products of peptic digestion of proteins participate directly in the mechanism of excitation of the intestinal phase of pancreatic secretion has not been definitely established up to the present time. This question has not been touched on in the investigations of I. P. Razenkov and his team of workers, nor has it been studied in detail by other investigators. A small number of experiments devoted to this question has shown that peptone, egg albumin, meat broth introduced into the stomach through a tube "do not exert a marked effect on the secretion of pancreatic juice and in most cases are either equivalent to water or even inferior to it with regard to stimulating secretion" (Dolinskii [1]).

On the other hand Thomas and Crider assert that the products of protein digestion, introduced directly into the intestine, exert a stimulating effect on the external secretion of the pancreas.

The literature data cited are not only conflicting but are also insufficiently convincing and cannot serve as proof of the stimulating action of the products of digestion on juice secretion, since in both cases the experiments were performed on dogs with normally functioning stomach, and the possibility of the introduced agents' stimulation of the pancreas being secondary to secretion of acid gastric juice was not excluded. Yet the question as to whether the products of peptic digestion can stimulate pancreatic juice secretion directly is of great significance both theoretically and in medical practise, since gastric resection and even total gastrectomy have become an extensively used surgical procedure.

The aim of our experiments has been the investigation of the changes occurring in the secretory activity of the pancreas as the result of gastric resection.

EXPERIMENTAL METHOD

The investigations were carried out on three dogs with exteriorized pancreatic ducts. The dogs were kept on a vegetable-milk diet and received daily from 2 to 3 g soda. The experiments were staged 18 hours after the last meal. The juice was collected by the Delezen method. The amount of juice secreted was noted every 15 minutes. Prior to administration of the stimulus the juice was collected over a period of one hour (arbitrary secretion according to Dolinskii) which served to establish the functional state of the secretory apparatus on any given day of experiment. The secretion norm was established to 100 g white bread, 100 g meat and 200 ml milk. The amount of juice and concentration of enzymes (amylase, trypsin and lipase) were determined in 1 ml of juice. Once the secretion norm was established the dogs were subjected to gastric resection by the Billroth II method in Hofmeister-Finsterer modification. From two-thirds to four-fifths of the stomach was resected. The period of observation lasted from 2 to 18 months.

EXPERIMENTAL RESULTS

The data obtained revealed that resection of the distal part of the stomach led to significant changes in the secretory activity of the pancreas, the degree and direction of these changes being related both to the kind of food stimuli employed and the time which had elapsed since operation. Thus, for example, the volume of secretion in response to bread used as a stimulus was markedly lowered for a period of about 4 months postoperatively, the decrease amounting to an average of 55-60%. The amount of juice then begins to increase reaching on some experimental days the initial values. However, this period is transient (about 3 months) and a more pronounced and persistent decrease of secretion in response to the given stimulus then supervenes. During this last period, which continues for over 10 months, the amount of juice is on average 15-25% less than the initial values before resection.

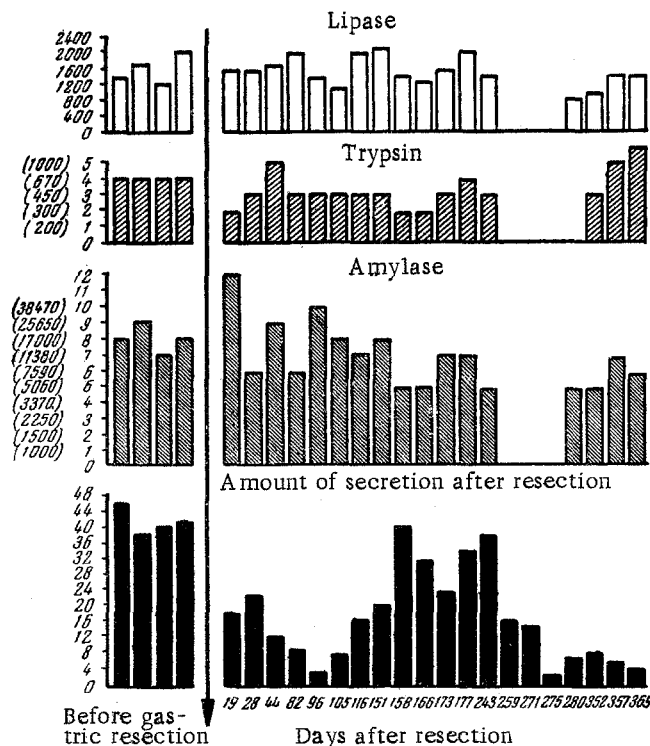


Fig. 1. Pancreatic juice and enzyme secretion by the pancreas in the dog Khudoi. Stimulus - Bread 100 g. The amount of pancreatic juice is represented by black columns; amylase concentration by columns hatched from left to right; trypsin by columns hatched from right to left; lipase by white columns; ↓ moment of gastric resection. At left along the ordinate are arbitrary units expressing the amount of enzyme in 1 ml juice.

Pancreatic Secretory Function in the Dog Lata (food stimulus milk 200 ml)

[illegible]

As regards the secretion of enzymes, amylase, trypsin and lipase, their concentration in the juice in most cases is in reverse relationship with the amount of juice secreted in unit time, i. e. as the rate of juice secretion drops there is a corresponding increase in unit time of concentration of the enzymes.

The following data are furnished as illustration (Fig. 1).

Quite a different picture is observed when milk is used as a stimulating agent. Since the data obtained on all three animals are basically identical, only the results obtained on one of them, the dog Lata, are given (Table 1).

Analysis of the material contained in the table indicates that pancreatic secretion in response to milk not only does not drop after resection but, with the exception of isolated experiments, even rises. Amylase concentration (the other enzymes were not determined in this dog) is lowered in isolated experiments which may be explained by increased hourly rate of juice secretion.

Juice secretion in response to meat, as that in response to bread, is lowered but not to the same degree in all the dogs. As in the case of bread and milk, the enzyme activity is related to the hourly rate of juice secretion.

It must be noted that the enzyme concentration, or enzyme activity, is not a reliable criterion for evaluation of the secretory activity of the pancreas unless the hourly rate of juice secretion is taken into account. The concept of enzyme-secretion, i. e. given concentration of enzyme multiplied by the hourly volume of juice secretion proposed by some workers is more meaningful. From this point of view factual material indicates that resection of the distal part of the stomach leads to marked lowering of the secretory activity (juice and enzyme) of the pancreas in response to bread and meat stimuli even in those cases in which the enzyme concentration is not decreased but rather somewhat increased, since the hourly volume of juice secretion is substantially decreased. The secretory activity of the pancreas is, on the contrary, increased in response to milk at least over a period of several months after gastric resection, although the concentration of amylase on isolated experimental days is somewhat diminished.

The data on the effect of milk on pancreatic secretory activity posed the question whether the facts observed in connection with decreased secretion in response to other stimuli (bread, meat) were the result of reduction of the functional possibilities of the pancreas itself as the consequence of transection during gastric resection of both vagi passing through the pylorus and duodenum to the pancreas, or whether the diminution of secretion in response to these stimuli depended on other causes.

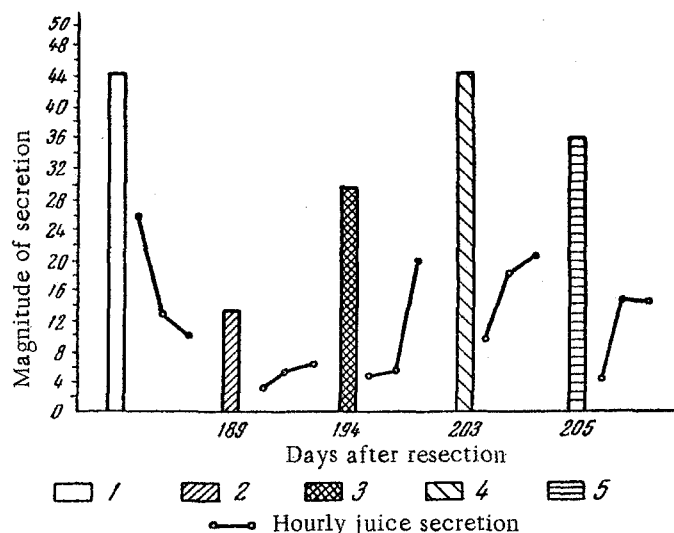


Fig. 2. Curves of pancreatic juice secretion before and after gastric resection.

- 1) Amount of juice in response to meat before gastric resection;
- 2) amount of juice in response to meat after resection; 3) amount of juice in response to meat + 30 ml gastric juice; 4) amount of juice in response to meat + 70 ml gastric juice following 18-hour digestion in thermostat; 5) amount of juice in response to meat + 70 ml gastric juice.

With this aim in view we undertook a series of experiments with meat and gastric juice added to it, as well as with products of peptic digestion of meat by gastric juice in a thermostat and their subsequent neutralization. The data obtained are presented in Figure 2. These indicate that before gastric resection the pancreatic juice secretion was 44 ml (typical experiment before resection), while on the 189th day after resection it was equal to only 14 ml. However, juice secretion in response to 100 g meat after its peptic digestion by gastric juice in a thermostat was the same as prior to resection.

In the experiment in which 100 g meat and 70 ml gastric juice were used the secretion of juice was increased but did not reach the initial value obtaining prior to resection. Attention is attracted by the character of the juice secretion curve. Before resection around 50 and over 50% of juice is secreted during the first hour, with a subsequent decline. After resection the situation is reversed: maximal amount of juice is secreted during the 3rd hour. This suggests that juice secretion is at this time effected chiefly by means of the intestinal phase of pancreatic secretion, i. e. as the result of entry of the products of digestion into the jejunum. The following experiments were performed by us in order to discover whether the products of protein digestion could have a primary stimulating effect (without the mediation of evoked gastric juice secretion) on pancreatic secretion after gastric resection by the Billroth II method, when they pass not into the duodenum but into the jejunum. A year and more after gastric resection a stomach stump fistula was made in one of the dogs in order to make it possible to control the reaction of its contents and to introduce food and other stimuli not per os, but directly into the cavity of the remaining part of the stomach.

The data obtained revealed that a 12% solution of peptone was able to evoke relatively large pancreatic secretion (Fig. 3). Figure 3 shows that 200 ml 12% peptone solution introduced into the cavity of the stomach stump evokes pancreatic juice secretion which is more than twice that evoked by a similar amount of water.

The question concerning the mechanism of pancreatic secretion in response to the introduction of HCl into the duodenum has not so far been clarified. It is all the more interesting that we have discovered that atropine (1.5-4 mg) given to the dog subcutaneously 15-45 minutes prior to administration of peptone produced a sharp decrease in the volume of pancreatic juice secretion elicited by the latter, with practically no change in enzyme activity, although the rate of juice secretion was considerably lowered and it might have been expected

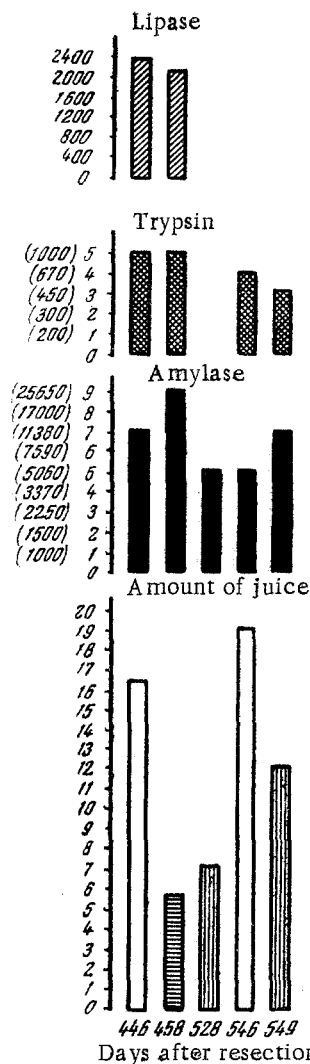


Fig. 3. Pancreatic secretion in response to peptone solution after gastric resection. White column - amount of juice secreted in response to stimulation with 12% peptone solution; horizontally hatched column - amount of juice secreted in response to water; columns with vertical hatching - amount of juice secreted in response to peptone solution after injection of atropine. Enzyme concentration is shown at the top of the figure. On the left along the ordinate are arbitrary units expressing the amount of enzymes in 1 ml juice.

function of the pancreas two-thirds to four-fifths of the stomach was resected in these dogs. The latter were observed for 18 months.

that there would be some increase in the concentration of enzymes in the jejunum.

It is difficult to postulate the mechanism for this phenomenon without further investigations, and particularly difficult when it is taken into account that under our experimental conditions the peptone passed not into the duodenum, with which pancreatic innervation is closely linked, but into the jejunum.

The factual material obtained leads to the conclusion that resection of the distal part of the stomach in dogs produces considerable changes in the secretory activity of the pancreas, their degree and direction being dependent both on the food stimuli used and on the time elapsed postoperatively.

The magnitude of juice secretion in response to bread is decreased by 55-60% for 3-4 months, then begins to increase reaching, on isolated experimental days, the initial values observed prior to resection. After 2-3 months a period of more drastic and persistent lowering of secretion sets in. During this period, already lasting for over 10 months, juice secretion amounts to 15-25% of the initial values. Enzyme concentration is near normal, and on isolated experimental days above it.

The magnitude of juice secretion in response to meat is lowered but not to the same extent in all the dogs. The amylase concentration is somewhat increased. The concentration of other enzymes fluctuates within normal limits.

Pancreatic juice secretion in response to milk is not only not decreased but is even either increased or within normal limits following gastric resection. The amylase concentration is slightly lowered and on isolated experimental days near to normal.

Addition of gastric juice to meat, as well as of products of peptic digestion of meat in a thermostat, elicit juice secretion which is near to normal, indicating that gastric resection does not, basically, diminish the functional capacities of the secretory apparatus of the pancreas.

Peptone solution introduced into the cavity of the stomach stump through a fistula elicits pancreatic juice secretion which is more than twice that elicited by the same amount of water.

Atropine inhibits the secretory activity of the pancreas elicited by peptone, decreasing the amount of juice secreted despite the fact that the concentration of enzymes is not altered substantially. All these data point to participation of a nervous mechanism in this process.

SUMMARY

This investigation was carried out on dogs in whom the pancreatic duct was exteriorized by surgical operation. The quantity of the juice and the concentration of the enzymes (amylase, trypsin and lipase) secreted in response to different stimuli were determined. After establishing the normal values for the secretory

The obtained data demonstrate that stomach resection causes considerable changes in the secretory function of the pancreas, the degree and the direction of which depended on the food stimuli, as well as on the period which elapsed after the resection. Peptone solution introduced into the cavity of the stomach stump through a fistula provoked pancreatic secretion, the quantity of which exceeded that caused by the same quantity of water by $2\frac{1}{2}$ times. Atropine is able to depress pancreatic secretion, decreasing its quantity, although there is no significant change in the concentration of the enzymes. These data demonstrate the participation of a nervous mechanism in this process.

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